

9/255 Response

**REMARKS**

As a result of this amendment, claims 1, 7, 8, 9, 12 have been amended. Claim 13 previously withdrawn has been rejoined. Claims 1-10, 12-13 are presently pending. In a telephone discussion with the Examiner and Applicants' attorney on 11/16/2004 it was agreed that claim 13 would be rejoined, claims 1, 7, 8, 9, 12 were deemed allowable in view of the above amendments, the evidence provided in the accompanying IDS and the discussion presented below. No new matter has been added to this application by way of amendment.

Using the THP cell assay and the p38 MAP kinase assay, page 52, the ordinary artisan can determine preferred compounds which inhibit TNF $\alpha$  production. The following literature articles provide the nexus between the activity and the claimed diseases:

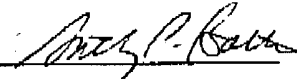
**Psoriasis:** G. Chodorowska, J. Eur. Acad. Dermatol. And Venesol., 1998, 10, 147, indicates that TNF $\alpha$  and INF- $\gamma$  have important roles in the inflammatory process of psoriasis.

**Chronic Obstructive Pulmonary Disease (COPD):** the major cause COPD is smoking. Less common are genetic factors which contribute to COPD. Certain genetic factors were studied by Higham et al. Eur Respir J 2000; 15:281-284 which concluded that while an association between the TNF2 allele and an increases risk of developing COPD was established in a male Taiwanese population, such a correlation was not demonstrated in a Caucasian population of smokers. Takabatake, N. et al. Am J Respir Crit Care Med. Vol 161 pp 1179-1184, 2000, obtained data suggesting that systemic hypoxemia noted in patients with COPD is associated with activation of the TNF $\alpha$  system in vivo.

**Rheumatoid Arthritis, Crohn's disease.** Early Alert Report, Fall 2000. This article reviews TNF $\alpha$  inhibitors, both biological and small molecule, and discusses their uses in the aforementioned diseases.

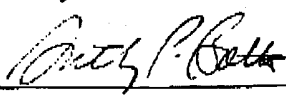
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Dated

Respectfully submitted,

  
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